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4	BRS	L4	260886	fast	USPAT	2003/07/25 11:37			0
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7	BRS	L7	1	1 and 4	USPAT	2003/07/25 11:39			0
8	BRS	L8	1	1 and 5	USPAT	2003/07/25 11:38			0
9	BRS	L9	0	1 and 6	USPAT	2003/07/25 11:39			0
10	BRS	L10	992	echo same (2-d or 3-d or dimension$1)	USPAT	2003/07/25 11:39			0
11	BRS	L11	1336	((mri or nmr) and imaging).ab,ti.	USPAT	2003/07/25 11:40			0
12	BRS	L12	73	10 and 11	USPAT	2003/07/25			0

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14	BRS	L14	23	13 and 11	USPAT	2003/07/25 11:48			0
15	BRS	L16	0	15 and 11	USPAT	2003/07/25 11:49			0
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25	BRS	L25	0	11 and 24	USPAT	2003/07/25 11:55			0
26	BRS	L26	25	24 not 15	USPAT	2003/07/25 11:55			0
27	BRS	L27	25	26 not 17	USPAT	2003/07/25 11:58			0
28	BRS	L28	22	planer near3 echo	USPAT	2003/07/25 12:04			0
29	BRS	L29	669	planar near3 echo	USPAT	2003/07/25 12:05			0
30	BRS	L30	2	(planar near3 echo) near10 (2-d or 3-d)	USPAT	2003/07/25 12:05			0
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33	BRS	L33	375	((2-d or 2-dimension$2) same (3-d or	USPAT	2003/07/25 12:08			0
34	BRS	L34	367	((2-d or 2-dimension$2)	USPAT	2003/07/25			0

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30	BRS	L30	2	(planar near3 echo) near10 (2-d or 3-d)	USPAT	2003/07/25 12:05			0
31	BRS	L31	176	(planar near3 echo) same (2-d or 3-d or	USPAT	2003/07/25 12:07			0
32	BRS	L32	176	31 not 24	USPAT	2003/07/25 12:06			0
33	BRS	L33	375	((2-d or 2-dimension$2) same (3-d or	USPAT	2003/07/25 12:08			0
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TITLE: Nuclear magnetic resonance imaging method and apparatus

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33	BRS	L33	375	((2-d or 2-dimension$2) same (3-d or	USPAT	2003/07/25 12:08			0
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37	BRS	L37	3	36 not 14	USPAT	2003/07/25 12:10			0
38	BRS	L38	11	((planar near3 echo) or epi or echoplanar) near10	USPAT	2003/07/25 13:01			0
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41	BRS	L41	101	((planar near3 echo) or epi or echoplanar) near10	USPAT	2003/07/25 13:06			0
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gradient fields, and that therefrom a two-dimensional nuclear magnetization distribution can be reconstructed. This method is referred to as the "echo-planar method" and is described in an article by P. Mansfield and I. L. Pykett, entitled "Biological and Medical Imaging by NMR", published in Journal of Magnetic Resonance, 29, 1978, pages 355-373, and also in an article by L. F. Feiner and P. R. Locher, entitled: "On NMR Spin Imaging by Magnetic Field Modulations", published in Applied Physics 22, 1980, pages 257-271. The echo-planar method utilizes time-dependent magnetic field gradients during the measurement of the FID signal. The echo-planar method enables a complete two-dimensional image to be obtained within the duration of a single FID signal. The determination of the nuclear magnetization distribution in a slice of the body to be examined is achieved by using, in addition to the uniform magnetic field, for example in the z-direction, for example, a magnetic field gradient G.sub.z in the same direction and at the same time a (90.degree.) high-frequency, amplitude-modulated pulse in order to generate an FID signal in a slice having an effective thickness .DELTA.z. Immediately after the

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	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef	R
93	☑	☐	US 4644383 A	19870217		Subcollector for oxide and junction isolated IC's	257/517	148/DIG.145; 148/DIG.37;	
94	☐	☐	US 4527124 A	19850702	19	Method of and device for determining a nuclear	324/309	324/307	
95	☐	☐	US 4509015 A	19850402	19	Nuclear magnetic resonance methods	324/309	324/307	
96	☑	☐	US 4508579 A	19850402		Lateral device structures using self-aligned	438/349	257/517; 257/557;	

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TITLE: Nuclear magnetic resonance imaging method

---------- KWIC ---------

Detailed Description Text - DETX (24):

This invention may be used in conjunction with many other types of pulse sequences to increase the efficiency of those techniques without sacrificing the unique advantages of those techniques. These methods include spin-warp imaging, two and three-dimensional Fourier transform imaging, Half-Fourier methods, echo-planar techniques, chemical shift imaging, etc. The higher the dimensionality of the technique the larger the efficiency gain by incorporation of the optimal sampling methodology of the invention.

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	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef	R
74	☐	☐	US 5119027 A	19920602	8	Nuclear magnetic resonance imaging method	324/309	324/307	
75	☐	☐	US 5079503 A	19920107	13	Magnetic resonance imaging apparatus and method for	324/309		
76	☑	☐	US 5077878 A	19920107		Method and device for passive alignment of diode	29/25.02	148/DIG.95	
77	☐	☐	US 5073752 A	19911217	12	Discrete Fourier transform imaging	324/309	324/312	

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US-PAT-NO: 5162736

DOCUMENT-IDENTIFIER: US 5162736 A

TITLE: NMR imaging

---------- KWIC ---------

Brief Summary Text - BSTX (4):

Despite the obvious advantages of EPI, there are particular problems in cardiac imaging. The heart moves in three dimensions not two and EPI being a two dimensional technique, is unable to follow object motions in and out of the imaging plane. This problem of motion along the third axis is exacerbated by respiratory motion. Of course third axis motion may be mitigated by

BRS form | IS&R form | Image | Text | HTML

	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef	R
72	☐	☐	US 5162736 A	19921110	14	NMR imaging	324/309		
73	☐	☐	US 5151656 A	19920929	13	Correction of NMR data acquired by an echo-planar	324/309	324/307	
74	☐	☐	US 5119027 A	19920602	8	Nuclear magnetic resonance imaging method	324/309	324/307	
75	☐	☐	US 5079503 A	19920107	13	Magnetic resonance imaging apparatus and method for	324/309		

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  - L4: (260886) f
  - L5: (1946648)
  - L6: (1430355)
  - L7: (1) 1 and
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Abstract Text - ABTX (1):

The invention provides a method of monitoring the vasodilatory or vasoconstrictive effects of a physiologically active substance administered t[o] a human or non-human animal body, said method comprising the steps of: administering said substance into said body; administering into the systemic vasculature of said body a contrast enhancing amount of an intravascular paramagnetic metal containing magnetic resonance imaging contrast agent; subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least a part of said body into which said agent passes, said procedure being a fast imaging procedure having an image acquisition time of less than five seconds; and detecting temporal variations in said signals or images whereby to monitor the vasoconstriction or vasodilation induced by said substance.

BRS form | IS&R form | Image | Text | HTML

	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef	R
1	☐	☐	US 5833947 A	19981110	15	Magnetic resonance imaging	424/9.36	424/9.363; 424/9.364;	

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Brief Summary Text - BSTX (11):

The method of the present invention is preferably carried out using spin-echo techniques. Alternatively and also preferably the method may be carried out using a so-called fast or ultra fast imaging technique in order enable a series of T.sub.2 * dependent images to be generated with as short as possible a time interval between successive images. For this reason, techniques capable of generating images with time intervals of less than 5 seconds, especially less than 0.5 seconds and more especially less than 100 milliseconds, are particularly preferred. Thus, in general, techniques such as spin echo, gradient echo, TurboFLASH, and most especially the various varieti of echo planar imaging (EPI), are particularly suitable for use in accordance with the method of the invention.

Brief Summary Text - BSTX (15):

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	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef	R
1	☐	☐	US 5833947 A	19981110	15	Magnetic resonance imaging	424/9.36	424/9.363; 424/9.364;	

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  - L7: (1) 1 and
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Brief Summary Text - BSTX (15):

In one embodiment of the method of the invention, using a fast imaging procedure, the determination of the location and severity of ischaemia is effected by determining the time dependence of the MR signal intensity for the voxels in the seconds following administration of the contrast agent, and generating an image where voxel image intensity value is dependent on the time post-administration at which MR signal intensity for that voxel is lowest. Normal tissue reaches minimum MR signal intensity sooner than ischaemic tissu and the resulting image thus enables the spatial extent and local severity of blood flow abnormality to be visualized. Alternatively, a similar image may l generated by making the voxel image intensity value dependent on the time tak before voxel MR signal intensity reattains a pre-selected control value, e.g. its pre-injection value or a percentage of that value (for example 80%).

Claims Text - CLTX (11):

BRS form | IS&R form | Image | Text | HTML

	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef	R
1	☐	☐	US 5833947 A	19981110	15	Magnetic resonance imaging	424/9.36	424/9.363; 424/9.364;	

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L13: (1632)
L14: (23) 1

Detailed Description Text - DETX (15):

Two and three-dimensional Fourier Transform (2-D FT and 3-D FT) methods are the most common MR image formation techniques currently in use. The Nuclear Magnetic Resonance (NMR) signal is digitally sampled using a phase sensitive detector, usually in phase and in phase quadrature. The image data is related to the signal or raw data, via a two or three-dimensional discrete Fourier Transform (2D-FT or 3D-FT), as described in, for example Callaghan, 1993, Chapter 3. In a 2D-FT sequence, denoting the signal as S(k.sub.x, k.sub.y,) and the image data as .rho. (x,y), where r denotes the position vector in image space, and k the vector in the conjugate Fourier space, the interrelationship between S(k.sub.x,k.sub.y) and .rho.(x,y) are as shown in equations 10 and 11:

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	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef	R
2	☑	☐	US 6422748 B1	20020723		Radiation therapy and radiation surgery treatment	378/203	250/505.1; 250/515.1;	
3	☑	☐	US 6249594 B1	20010619		Autosegmentation/autocontouring system and method	382/128		
4	☑	☐	US 6236738 B1	20010522		Spatiotemporal finite element method for motion	382/107		
5	☐	☐	US 6150814 A	20001121	22	Methods of achieving phase contrast in magnetic	324/307	324/309	

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  - L12: (73) 1
  - L13: (1632)
  - L14: (23) 1
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Brief Summary Text - BSTX (9):

CT imaging and MRI are two of the most frequently used imaging modalities because both provide detailed pictures of the internal anatomy of a patient. The instruments that employ these imaging techniques provide data that in appearance is 2-D or 3-D. However, the 3-D images, as stated, are a collection of 2-D samples, in this form of slices or sections, of the anatomy that have been combined to create a 3-D images. More specifically, to recreate the 3-D images from the 2-D image samples, the physician, scientist, or other skilled professional must recombine the 2-D image samples (slices or sections) of the anatomic elements (organs, tumors, surgically-implanted prostheses, etc.) A common way to recombine 2-D image samples to form 3-D images is to manually draw individual contours on a contiguous set of 2-D image slices or sections using computer graphics. Once these manually drawn contours are made, they are assembled to accurately construct 3-D representations of organs, tumors, and the like. The resulting 3-D reconstructions convey to the viewer the relative sizes, shapes, and mutual spatial relationships among the anatomic elements in the same anatomical scale as the original.

Brief Summary Text - BSTX (11):

As stated, 3-D reconstructions of patient anatomy are most often prepared using computer graphics by manually drawing the individual contours on a contiguous set 2-D image slices or sections and then combining them. This

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	U	1	Document ID	Issue Date	Pages	Title	Current OR	Current XRef	R
2	☑	☐	US 6422748 B1	20020723		Radiation therapy and radiation surgery treatment	378/203	250/505.1; 250/515.1;	

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Within 3–5 hours after MCA occlusion, T_2-weighted images also demonstrated tissue injury clearly, including increased mass-effect and hyperintensity (edema) throughout the MCA territory. The distribution of increased signal intensity correlated well anatomically with regions of perfusion deficiency demonstrated with DyDTPA-BMA-enhanced MR imaging. A continuing close anatomic correspondence between areas of perfusion deficit and edematous regions was seen 9 hours and 11 hours post occlusion. In subsequent TTC-stained coronal sections, these areas were found to exhibit characteristics typical of ischemic tissue injury, such as pallor of staining, coagulation necrosis, and glial proliferation.

These results confirm that MS contrast agent enhanced MRI can significantly advance the time of detection of cerebral ischemic insults. Evidence of stroke-induced perfusion deficits was observed in the MCA territory as early as 45 minutes post-occlusion using contrast-enhanced MRI, whereas T_2-weighted spin-echo images without contrast did not demonstrate increased signal intensity until 2–3 hours after occlusion.

Contrast in T_2-weighted spin-echo MRI can be produced by changes in the microscopic magnetic fields experienced by protons undergoing molecular diffusion. These field gradients cause spin dephasing and loss of spin echo signal intensity. Field gradients arise at the interface of two volumes with different magnetic susceptibilities and thus different induced magnetic fields.

The presence of paramagnetic chelates can alter the magnetic susceptibility of tissue. In the brain, since the chelates are confined to the intravascular space by the blood-brain barrier, a field gradient is induced between the capillary space and surrounding (perfused) tissue resulting in significant signal loss. These results show that this approach to MR contrast enhancement can be used to differentiate ischemic from normally perfused regions.

A further notable advantage of the method of the

ing in conjunction with low, 0.1 mmol/kg, doses of DyDTPA-BMA, we have found that quantitative spatial and temporal assessment of stroke affected tissue may be made. This dosage reduction further increases both the potential sensitivity and the safety profile of the method of the invention.

The advantage of using echo planar MRI with a MS contrast agent is that images may be acquired continuously before, during and after contrast injection. This allows the time course of the contrast agent passage through a tissue to be monitored and to obtain images at the maximum contrast dosage.

Echo planar images on the GE CSI 2 Tesla were acquired in a sequential fashion. Sixteen images were obtained one each second or less, each image possessing a 66 msec acquisition time with a data matrix of 64×64 pixels over a 60×60 mm field-of-view. The slice thickness was 3 mm. The echo-planar sequence was that of a gradient-echo nature, with the time of echo (TE) value adjusted to maximize the T_2^*-shortening contrast effect.

What is claimed is:

1. A method of detecting regions of blood flow abnormality or variation in a human or non-human body, said method comprising the steps of (1) administering into the cardiovascular system of said body a contrast enhancing amount of a paramagnetic metal containing magnetic resonance imaging contrast agent, (2) subjecting said body to a magnetic resonance imaging procedure and obtaining a series of temporally spaced magnetic resonance signals or images from regions in at least a part of said body into which said agent passes, (3) detecting temporal variations in said signals or images, and (4) identifying from said temporal variations in said signals or images regions of abnormal or modified blood flow in said body and providing a quantitative indication of the degree of blood flow abnormality or modification therein.

2. A method of detecting and quantitatively evaluating the severity and spatial extent of ischemic regions in a human or non-human body, said method comprising the steps of (1) administering into the cardiovascular system of said body a contrast enhancing amount of a

phase encoding steps 32 and 60 of the 128 phase encoding-step acquisitions. FIGS. 23*a*, *b* and *c* and 24*a*, *b* and *c* show the recorded images at 128 and 280 minutes (the (a) images), the contour maps of hyperintensity (the (b) images showing the reference areas (100%) of the unaffected hemisphere) and the superpositions of the MR images and the contour maps (the (c) images). At 128 minutes seven different regions of perfusion deficiency were identified. This heterogenicity of the perfusion deficiency is to be expected early in the course of a cerebral ischaemia. At 280 minutes the increased levels of hyperintensity confirm worsening perfusion deficit in most brain regions but the heterogeneity of the hyperintensity suggests that some brain areas may still retain some blood flow.

We claim:

1. A method of monitoring the vasodilatory or vasoconstrictive effects of a physiologically active substance administered to a human or non-human body, said method comprising the steps of: administering said substance into said body; administering into the systemic vasculature of said body a contrast enhancing amount of an intravascular paramagnetic metal containing magnetic resonance imaging contrast agent; subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least a part of said body into which said agent passes, said procedure being a fast imaging procedure having an image acquisition time of less than five seconds; and detecting temporal variations in said signals or images whereby to monitor the vasoconstriction or vasodilation induced by said substance.

2. A method according to claim 1 wherein said contrast agent comprises a physiologically tolerable complex of a paramagnetic lanthanide ion or a physiologically tolerable salt of such a chelate.

3. A method according to claim 2 wherein said contrast agent is a chelate complex of a metal ion selected from the paramagnetic ions of Yb, Tm, Dy, Ho, Er and Gd, or a physiologically tolerable salt thereof.

4. A method according to claim 3 wherein said contrast agent is a chelate complex of Dy(III) or a physiologically tolerable salt thereof.

11. A method according to any one of claims 1, 2, 4 or 8 wherein said procedure is one having an image acquisition time of less than 0.5 seconds.

12. A method according to any one of claims 1, 2, 4 or 8 wherein said procedure is an echo planar imaging procedure.

13. A method according to any one of claims 1, 2, 4 or 8 wherein administration of said contrast agent is by bolus injection.

14. A method according to any one of claims 1, 2, 4 or 8 comprising generating temporally spaced T_2* or T_2-weighted images.

15. A method according to claim 14 wherein said magnetic resonance imaging procedure is a spin-echo or gradient echo procedure.

16. A method according to claim 14 comprising generating and comparing T_1-weighted images or signals transformable thereto and T_2* or T_2-weighted images or signals transformable thereto whereby to identify body regions in which blood perfusion occurs.

17. A method according to claim 1 being a method of detecting body regions of blood flow deficit in which blood perfusion is thermally or chemically modified.

18. A method according to claim 1 wherein said contrast agent comprises a physiologically tolerable complex of a paramagnetic transition metal ion or a physiologically tolerable salt of such a chelate.

19. A method according to claim 8 wherein said contrast agent is administered as a contrast medium composition comprising DyDTPA-BMA and CaNaDTPA-BMA in a molar ratio of about 20:1.

20. A method of monitoring the vasodilatory or vasoconstrictive effects of a physiologically active substance administered to a human or non-human animal body said method comprising administering said substance into said body, administering into the systemic vasculature of said body a contrast enhancing amount of an intravascular paramagnetic metal containing magnetic susceptibility magnetic resonance imaging contrast agent, subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series

the reference areas (100%) of the unaffected hemisphere) and the superpositions of the MR images and the contour maps (the (c) images). At 128 minutes seven different regions of perfusion deficiency were identified. This heterogenicity of the perfusion deficiency is to be expected early in the course of a cerebral ischaemia. At 280 minutes the increased levels of hyperintensity confirm worsening perfusion deficit in most brain regions but the heterogeneity of the hyperintensity suggests that some brain areas may still retain some blood flow.

We claim:

1. A method of monitoring surgically induced blood perfusion variations, said method comprising administering a contrast enhancing amount of an intravascular paramagnetic metal containing magnetic susceptibility magnetic resonance imaging contrast agent into the systemic vasculature of a human or animal body which is undergoing or has undergone surgery, subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least a part of said body into which said agent passes, and detecting temporal variations in said signals or images whereby to identify regions of surgically induced variations in blood perfusion.

2. A method according to claim 1 wherein said contrast agent comprises a physiologically tolerable complex of a paramagnetic lanthanide ion or a physiologically tolerable salt of such a chelate.

3. A method according to claim 2 wherein said contrast agent is a chelate complex of a metal ion selected from the paramagnetic ions of Yb, Tm, Dy, Ho, Er and Gd, or a physiologically tolerable salt thereof.

4. A method according to claim 3 wherein said contrast agent is a chelate complex of Dy(III) or a physiologically tolerable salt thereof.

5. A method according to claim 1 wherein said contrast agent comprises a physiologically tolerable non-ionic paramagnetic lanthanide chelate complex.

6. A method according to claim 2 wherein said chelate complex is a complex of a linear, branched or macrocyclic chelant selected from polyaminopolycarboxylic acid

9. A method according to claim 1 wherein said contrast agent is administered at a dosage of 0.02 to 3 mmol/kg bodyweight.

10. A method according to claim 1 wherein said contrast agent is administered at a dosage of 0.08 to 0.5 mmol/kg bodyweight.

11. A method according to claim 1 wherein said magnetic resonance imaging procedure is a fast imaging procedure.

12. A method according to claim 11 wherein said fast imaging procedure is one having an image acquisition time of less than 5 seconds.

13. A method according to claim 11 wherein said fast imaging procedure is one having an image acquisition time of less than 0.5 seconds.

14. A method according to claim 1 wherein said magnetic resonance imaging procedure is an echo planar imaging procedure.

15. A method according to claim 1 comprising generating temporally spaced T_2* or T_2-weighted images.

16. A method according to claim 15 wherein said magnetic resonance imaging procedure is a spin-echo or gradient echo procedure.

17. A method according to claim 15 comprising generating and comparing T_1-weighted images or signals transformable thereto and T_2* or T_2-weighted images or signals transformable thereto whereby to identify body regions in which blood perfusion occurs.

18. A method according to claim 1 being a method of detecting body regions of blood flow deficit.

19. A method according to claim 18 being a method of detecting ischemic regions.

20. A method according to claim 1 wherein said contrast agent comprises a physiologically tolerable complex of a paramagnetic transition metal ion or a physiologically tolerable salt of such a chelate.

21. A method according to claim 1 wherein said contrast agent is administered as a contrast medium composition comprising DyDTPA-BMA and CaNaDTPA-BMA in a molar ratio of about 20:1.

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